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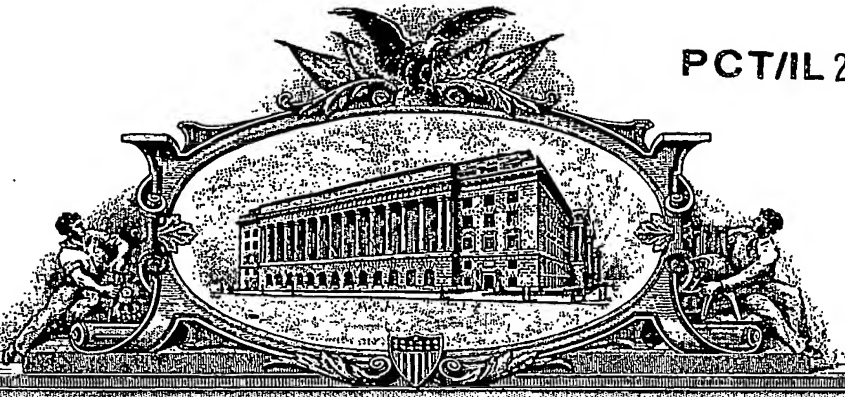

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APPLICATION NUMBER: ***60/516,613***
FILING DATE: ***October 30, 2003***

By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a requ st for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

22151 U.S.PTO 60/516613 103003

INVENTOR(S)		
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[X] *Additional inventors are being named on the 1 separately numbered sheets attached hereto.*

TITLE OF THE INVENTION (280 characters max)

DRUG MIXING DEVICE FOR INTRAVENOUS DELIVERY

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

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ENCLOSED APPLICATION PARTS (*check all that apply*)

[X] Specification *Number of Pages* 8 [ ] CD(s), Number

[X] Drawing(s) *Number of sheets* 30 [ ] Other (specify)

[ ] Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT (check one)

[X] Applicant claims small entity status. See 37 CFR 1.27.

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FILING FEE AMOUNT ($) $80.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

[X] No.

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Respectfully submitted,

SIGNATURE _____

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Date: October 30, 2003

REGISTRATION NO. *(if appropriate)* 24,156

Docket Number: 206,320

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

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PROVISIONAL APPLICATION COVER SHEET
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Docket Number	206,320	Type a plus sign (+) inside this box →	+

INVENTOR(S) APPLICANT(S)		
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DRUG MIXING DEVICE for INTRAVENOUS DELIVERY

INTRODUCTION

Drugs for intravenous infusion are usually introduced into an infusion solution container in the following manner:
A volume of solution is withdrawn from the solution container by a syringe equipped with a needle. The solution is injected into a drug containing vial, and the drug is dissolved in the solution by shaking. A New needle is connected to the syringe, and some or all of the dissolved drug is withdrawn from the vial and injected into the infusion solution container.

This procedure is cumbersome, and when handling cytotoxic drugs – dangerous as well. Therefore improvements were sought to make the procedure safer. A number of products have been introduced addressing this issue. A leading product, Phaseal, is made by Carmel Pharma, Goteborg, Sweden. B. Braun, Germany, and Codan, Germany, have also introduced products in this area.

A common feature of all these products is that the syringe used is either needle-less or has a needle protection mechanism. Still, in all these products a drug filled syringe is physically transported from the vial to the infusion solution container. In the B. Braun and Codan devices the drug filled syringe is open to the atmosphere during the transition from vial to container. The Pheseal system provides better protection but is cumbersome and expensive. A device is therefore needed which is safe, simple to use and inexpensive.

SPECIFICATION

The drug mixing devices of this invention simultaneously connect all the components necessary for effecting the transfer of a known amount of drug from a drug container to an IV solution container. Said components can be either

a. Drug container and solution container

or

b. Drug container, solution container and volume measuring device such as syringe.

In the system embodiments described below, means are provided for introducing into the system a volume of sterile air necessary for unimpeded transfer of solution from the solution container to the drug container and back into the solution container.

The whole transfer and mixing procedure is done in a closed system.

System components common to the devices of this invention are:

1. Drug container connection means

2. Solution container connection means

3. A membrane vent for controlled system pressure equalization. The vent is preferably a hydrophobic membrane, having a pore size suitable for retention of air-borne bacteria and having a surface area sufficient to allow fast air introduction into evacuated drug containers and air expulsion from drug containers upon filling.

In some embodiments, means are provided for distributing the drug contained in one drug container into more than one solution container. In some embodiments the drug container is provided with protective packaging connecting onto the drug mixing device, thereby obviating the need to remove the container from the packaging.

The devices of this invention will now be described in detail referring to the following figures:

Figure 1. Mixing device A

Figure 1A Mixing device A cross section

Figure 2. Assembled system with device A

Figure 2A. Mixing device A with alternate delivery port

Figure 3. Mixing device B

Figure 3A Vent construction, mixing device B

Figure 4. Assembled system with device B

Figure 26. Protective packaging C and assembled mixing device

Figure 27. Protective packaging C with pierced vial

Referring to Fig. 1, mixing device A is a device suitable for transferring the whole content of a vial into a single solution bag. The device includes a vial connector spike and shroud (1) and solution bag connection means (2). Connection means (2), connects to a bag spike (Figure 7) that had previously been connected to a solution bag. Connection is through piercable septum (3) in the bag spike.

Operation of this system is as follows:
Clamp 4 (Figs 2, 7) on the delivery line is closed. The system is positioned first with the solution bag on top and drug vial below. The bag is squeezed to push some solution into the vial. Displaced air from the vial moves into the bag. The vial is shaken to dissolve the drug. The system is then turned 180^0 so that the vial is on top (Fig. 2). Squeezing the bag in this position, forces air from the bag into the vial, the air in turn forcing the liquid in the vial back into the bag. To ensure complete drug transfer, the above sequence may be repeated. Once completed, the solution bag is ready for drug delivery.

A unique feature of device A is the venting mechanism shown in Fig. 1A. Intravenous solution bags contain a certain volume of air. This volume is not very accurately controlled by bag manufacturers. The transfer mechanism described above requires a minimum air volume for efficient operation. When connecting a solution bag with low air volume to an evacuated drug vial, all air may disappear and make the solution transfer impossible. Therefore the membrane vent (5) is designed such that air enters the vial immediately upon piercing by spike (1). When solution is first transferred from the solution bag to the vial, venting passage (6) fills with liquid. As passage (6) is relatively long and narrow, liquid is retained in it by capillary force throughout the subsequent procedure. Thus, after first system venting, the venting membrane is effectively plugged, thereby trapping all air in the system. This ensures that the proper volume of air is available for operating the system.

The connection means between mixing device and bag spike is shown in Figures 1, 1A and 2. A needle (7) covered with an elastomeric sheath (8) is fixed in a protective shroud (9). This needle assembly is simply pushed

onto the injection site on the bag spike (3). Upon piercing the injection site by needle (7), the elastomer sheath recedes and locking tabs (10) lock onto a recess on the injection site. For release of the mixing device from the bag spike (if desired), one depresses the tabs (10, Fig 2) and pulls the device off. Needle 7 thereby exits from injection site (3, Fig 7) and is automatically recovered by sheath 8, preventing solution drip.

An alternate design for the bag spike is shown in Fig. 2A. Here, instead of tubing leading to manifold or stopcock (Fig.7), the bag spike has a spike-piercing site (4a) into which any standard delivery set can be connected.

Figure 3 shows a second embodiment of the current invention wherein the mixing device comprises drug vial connection means (1), bag spike connection means (2) a port for a volume measuring and transfer means, such as a syringe (11), a flow control means such as stopcock (12) and venting means (13). The venting mechanism, shown in detail in Fig. 3A, is different from that of the first embodiment (5, Fig. 1A).

In the current embodiment air must be allowed to enter the system when the drug vial is evacuated, and to be expelled when the vial is filled (see below). Therefore the inside of the drug vial communicates with the external atmosphere through channel (14, Fig. 3A) and hydrophobic membrane (15). The system of this embodiment, shown assembled in Fig. 4, is designed for solution transfer by syringe , and is especially suitable for drug vials that are only partially mixed into solution bags, or vials that are distributed into more than a single bag. Operating this system is as follows:

1. The system is assembled by connecting a bag to a bag spike and the mixing device to the bag spike injection port. A drug vial is connected to the vial connecting means of the mixing device. If the vial is evacuated, pressure in the vial is automatically equalized by the membrane vent.

2. The system is positioned with the solution container on top and vial below (see Fig. 4). The stopcock is positioned such that the drug vial is plugged and there is fluid communication between solution container and syringe.

3. A measured volume of solution is drawn from the bag into the syringe.

4. The stopcock handle is moved to a second position providing communication between syringe and vial (and preventing communication between syringe and solution container) and the contents of the syringe is emptied into the vial. Air is expelled from the vial through the vent.

5. After dissolving the drug the system is turned 180^0 so that the vial is on top (Fig.5).

6. Without changing the position of the stopcock handle a measured volume of dissolved drug is drawn from the vial into the syringe. Sterile air enters the vial through the vent to equalize pressure.

7. The stopcock is turned to its original position and the syringe is emptied into the solution bag.

8. The mixing device with vial and syringe is removed from the solution container and spike by pressing on the tabs (10, Fig.6) and pulling off.

The bag is now ready for infusion delivery, and the mixing device is ready for connection to a second bag.

Means can be provided such that a single size mixing device will fit all available drug vial sizes. Drug vials come in various volumes, but have only few cap sizes. Since the mixing devices of embodiments described thus far attach to the vial cap and neck only, the volume and shape of vial body are immaterial.

Figure 8 shows the largest cap vial connected directly to the mixing device. For smaller cap vials, an adaptor is first attached to the vial cap as shown in Figure 9. This vial-adaptor assembly is then snapped into the standard sized mixing device as shown in Figure 10.

A number of alternate modes for connecting the mixing device to a solution container are possible. In one mode, shown in Figure 11, the mixing device includes a needle assembly (14) (shown without mixing device). The needle assembly comprises a sharp needle (15), elastomer

sheath (16) and flexible plastic arms (17) surrounding the sheathed needle. The needle assembly is snapped onto a solution bag injection site (18). During connection the needle pierces the injection site, the elastomer sheath receded and the flexible arms lock onto a recess on the injection site (Figure 12). Upon disconnection (effected by pulling the mixing device off the injection site) the sheath (16) springs back to recover the needle and prevent solution spillage.

In another connection mode, the mixing device needle assembly is as shown in Figure 13. A needle (19) is fixed to a needle mount (20). The needle mount is moveable relative to an elastomeric septum (21) fixed in a housing with flexible arms (17). In use, the mixing device is pushed onto the bag injection site (18), as in the previously described connection mode. This results in the connected configuration, shown in Figure 14. Now the mixing device and needle are advanced relative to the injection site, thereby piercing it, as seen in Figure 15. For disconnection of mixing device from bag, the above steps are reversed, thereby returning the needle tip to its protected position inside elastomeric septum (21, Fig. 13).

For certain drugs, especially cytotoxic drugs, it is desirable to have protective packaging, protecting the drug container against breakage and protecting the environment against spillage of toxic drugs. Such drugs are usually delivered via intravenous infusion. It would be desirable that when delivered in a protective packaging, drug vials do not need to be removed from said packaging in order to dissolve the drug in an infusion solution.

The embodiments shown in Figures 16 to 26 address this need.

Figure 16 shows a vial inside protective packaging, having a body (22) and cap (23). The body has a built-in external thread for connecting said body to the cap or to the mixing device. In use the cap is removed and a mixing device, a detail of which is shown in Figure 17 is threaded on. The mixing device has a vial piercing spike as previously described, fixed inside an open cylinder with internal thread. Threading the above vial-in-packaging into the structure of Fig. 17 causes the spike to penetrate the vial stopper. This results in the assembly shown in Figure 18 with pierced vial inside the protective package. The system is now ready for use in either of the two modes described previously (with or without flow control means such as stopcock). Other, non threaded vial advance mechanisms are possible.

Another mode of protecting and using a drug vial is shown in Figure 19. Here the packaging consists of three parts: Body (24), top (25) and cap (26). The cap includes vial stabilizing rib (26A). While in the mode of Figure 16 various mixing device sizes must be made for various vial body sizes, the current mode enables the use of a single-size mixing device for all vial sizes. As shown, the thread in this mode is not on the body but on the top, which is of a length approximately equal to that of the vial neck and cap. While the dimensions of body (24) will vary according to the dimensions of the various vials, the dimensions of the top (25) are fixed. The internal diameter of the top is somewhat larger than that of the largest vial cap. The top may have a recess (27, Fig 20) for removing the plastic vial cap without removing the vial from its packaging.

In use, packaging cap (26) is removed, exposing vial cap (28, Figure 21). The vial cap is removed by pushing up with a finger or nail along recess (27). Then the mixing device, having an internal thread, is threaded onto the open vial package, thereby piercing the vial stopper (Figure 22). An assembled system is shown in Figure 23. Drug is transferred from the vial into the solution bag in either of the previously described modes (with or without stopcock).

Yet another packaging mode is shown in Figure 24. Here too the packaging comprises a body (29) top (30) and cap (31). Here too a single mixing device is suitable for all vial sizes. The cap is removed, enabling removal of the vial cap, as shown in Figure 25. The top (30) is also removed and snapped into a mixing device (Figure 26) having a spike, but devoid of threaded cylinder (Figure 26). Upon rethreading the mixing device-top assembly onto the body, the spike penetrates the vial stopper (Fig. 27).

The system is now ready for use as previously described.

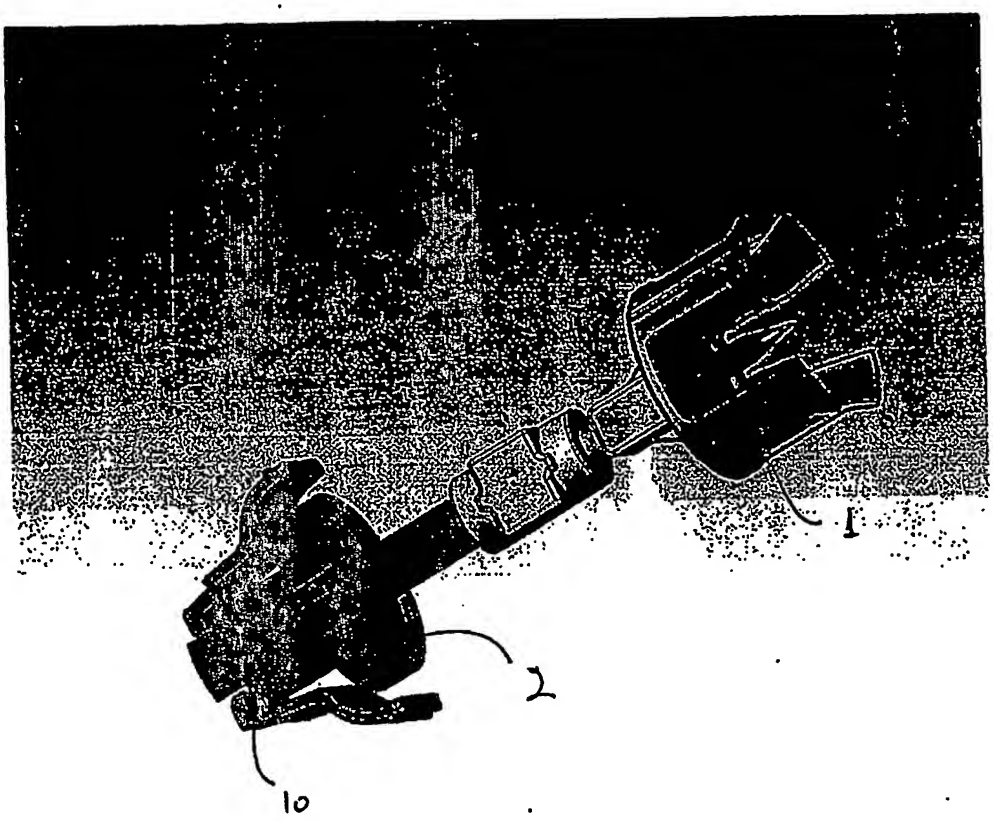


Figure 1.

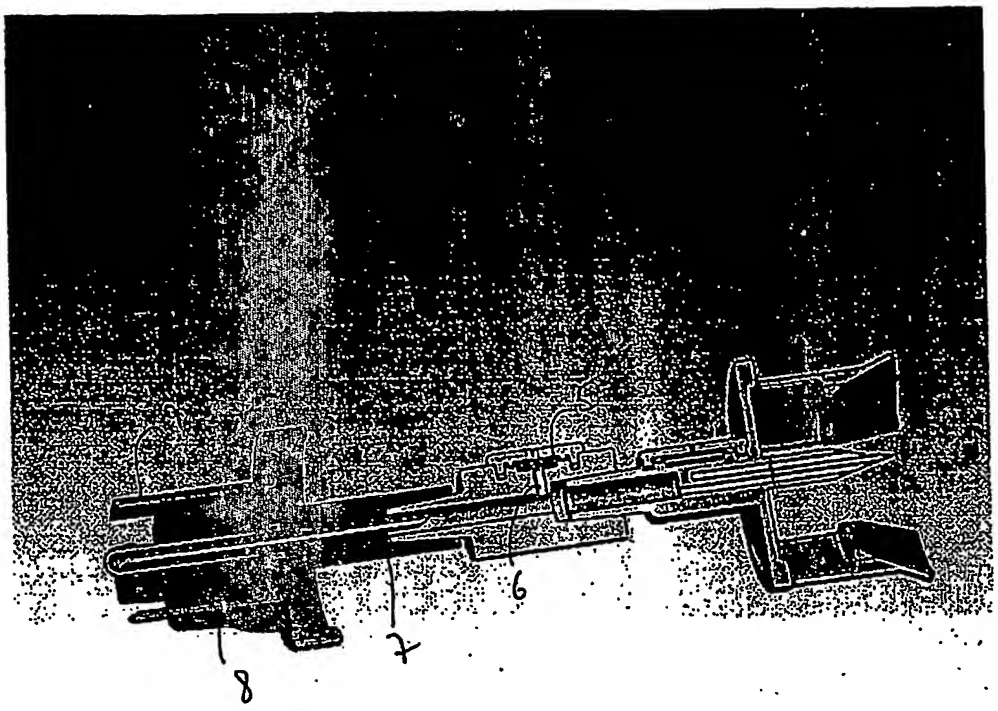


Figure 1A

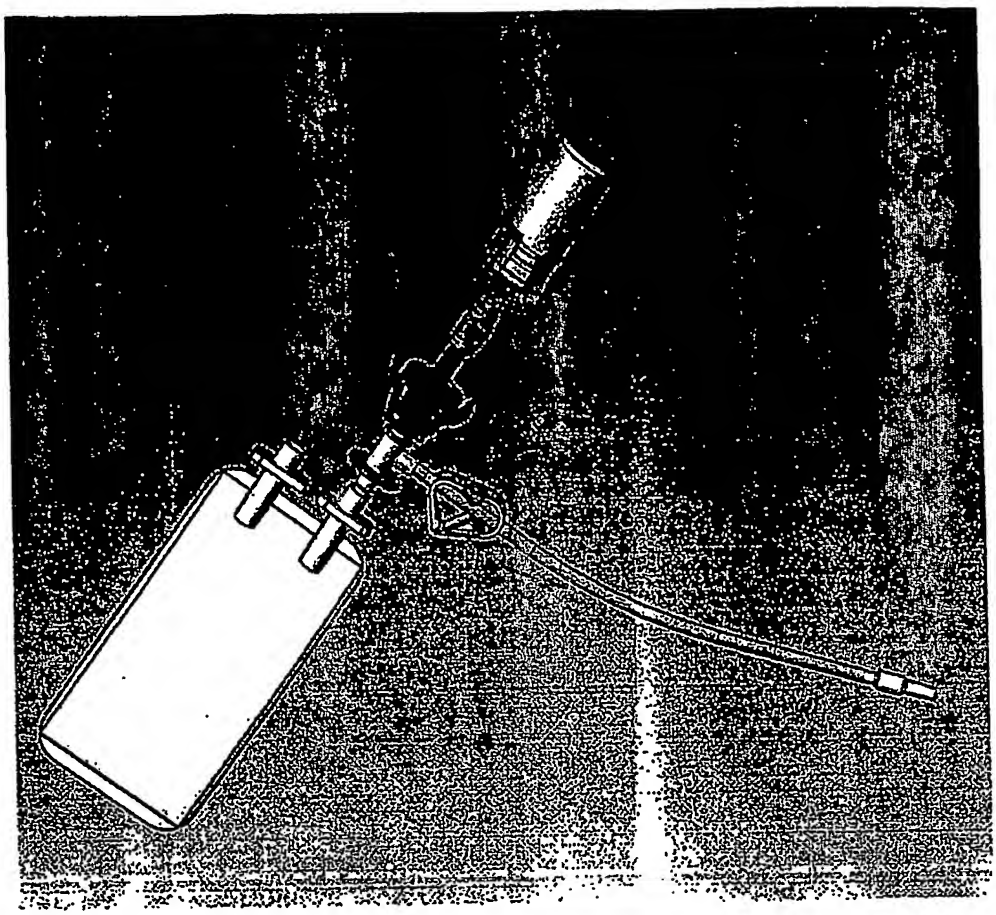


Figure 2

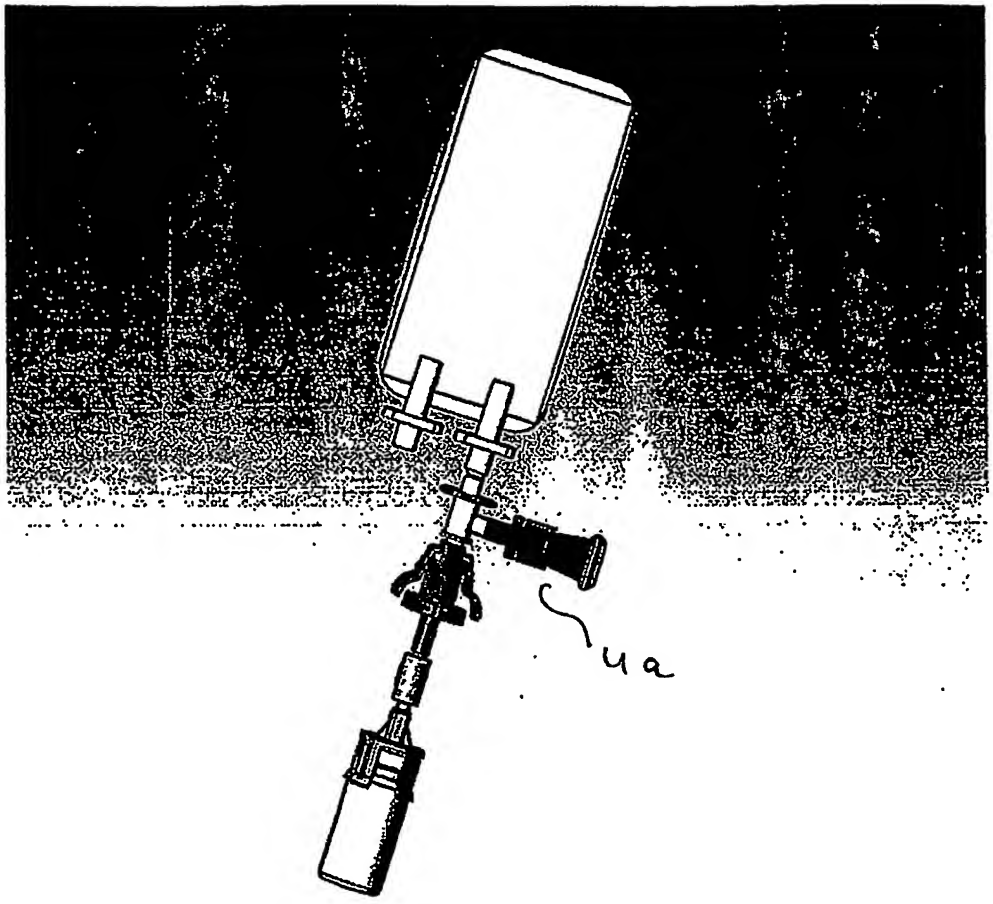


Figure 2A

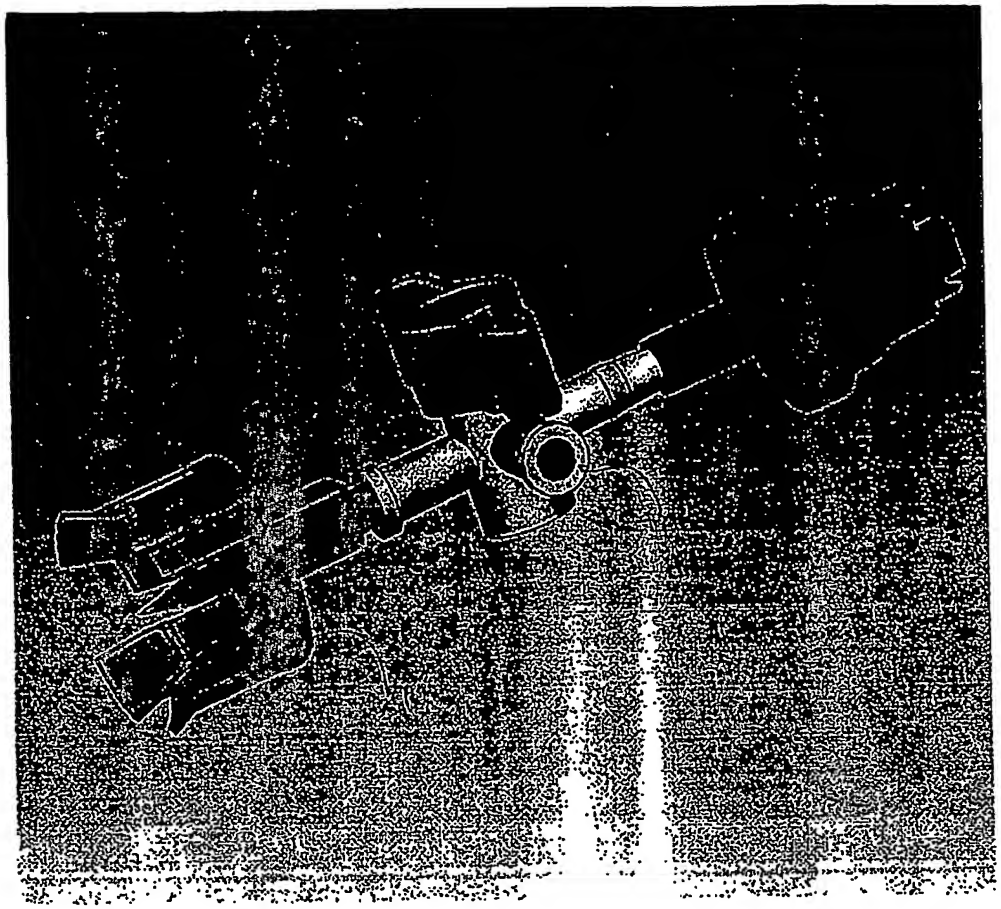


Figure 3.

Figure 3A

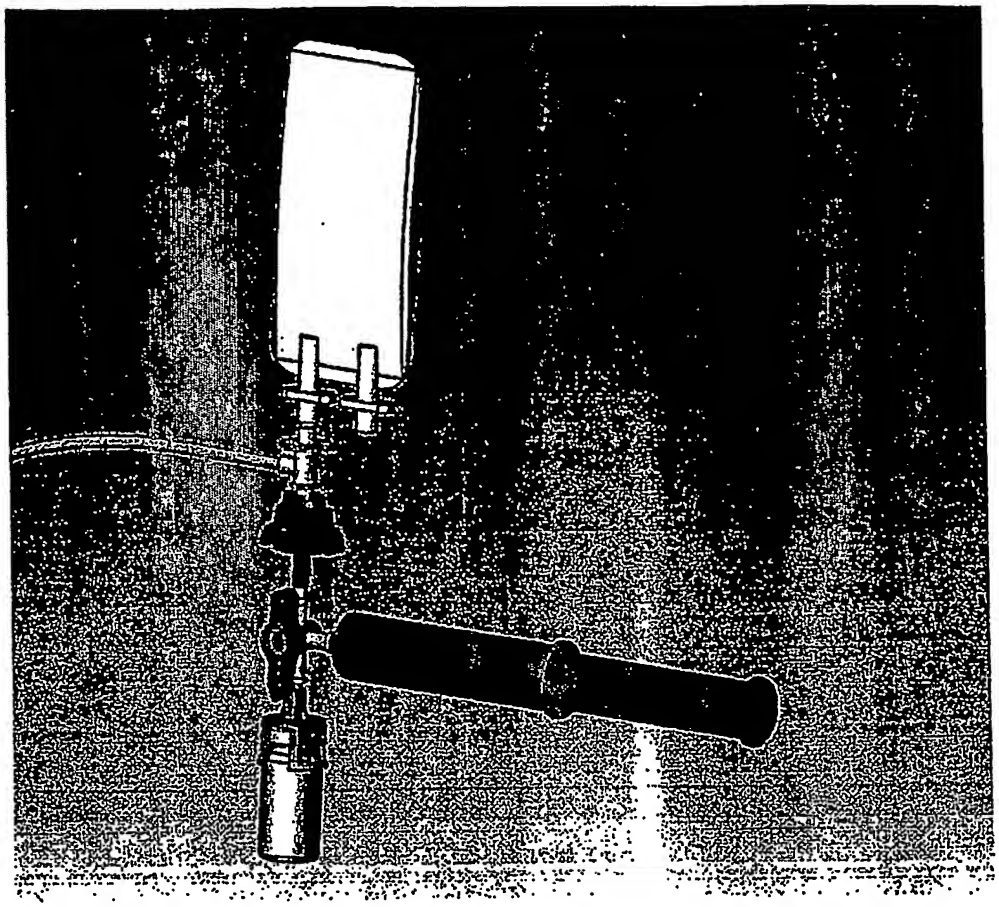


Figure 4

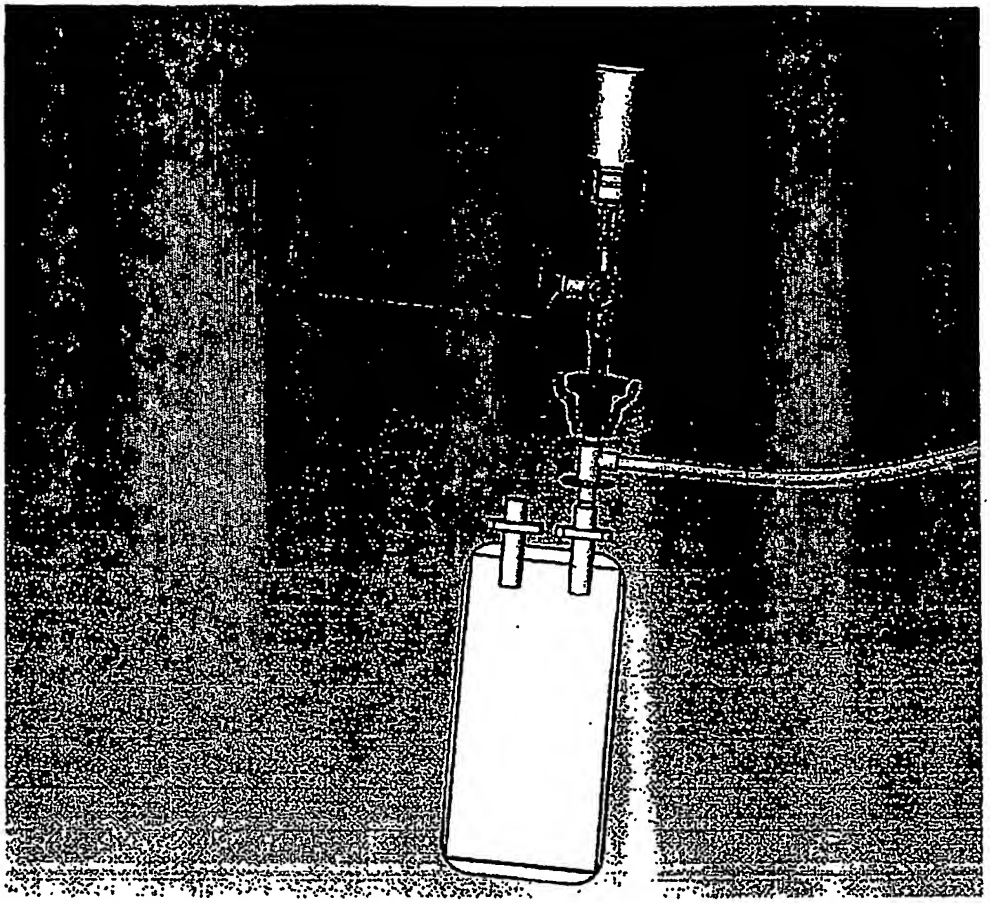
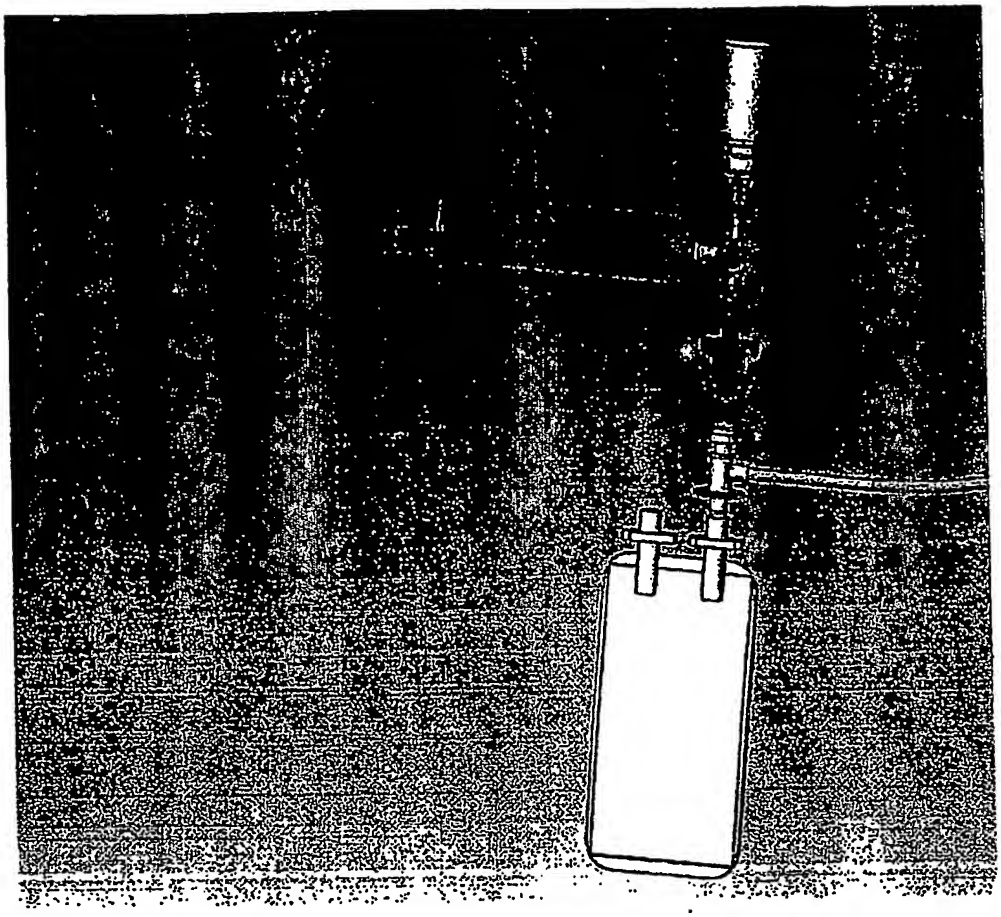


Figure 5



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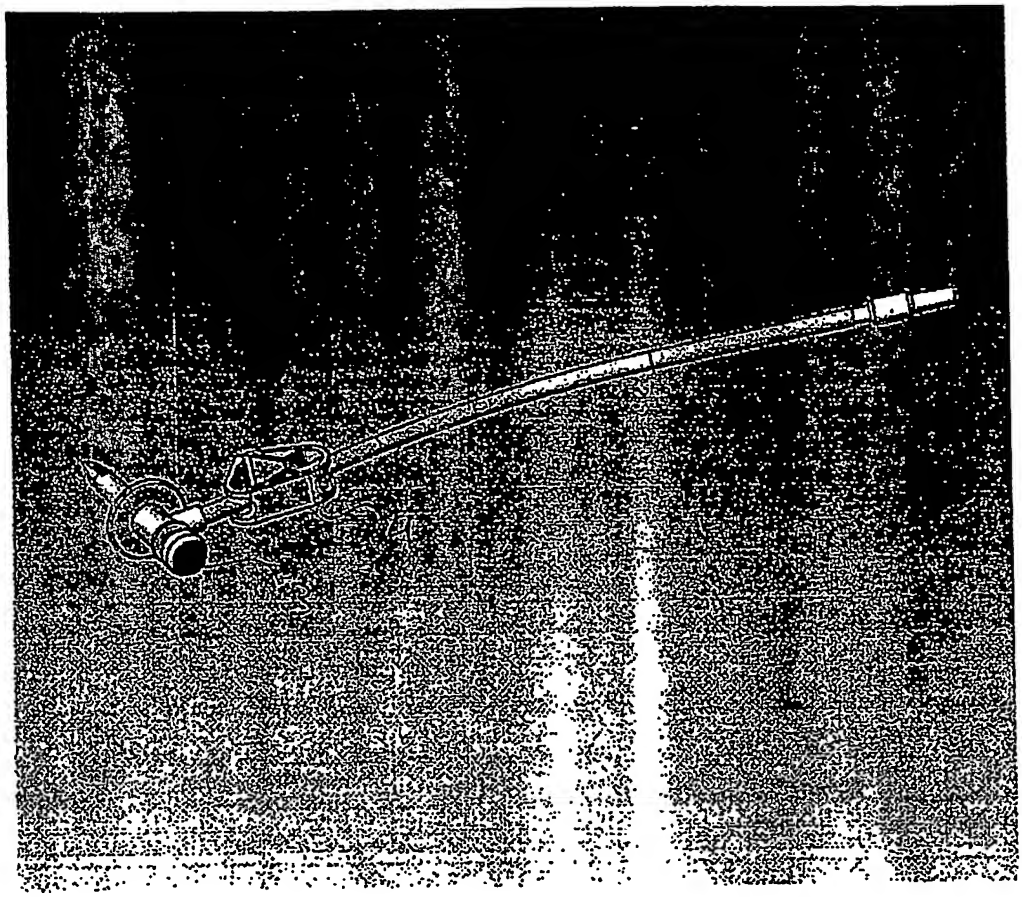


Figure 7

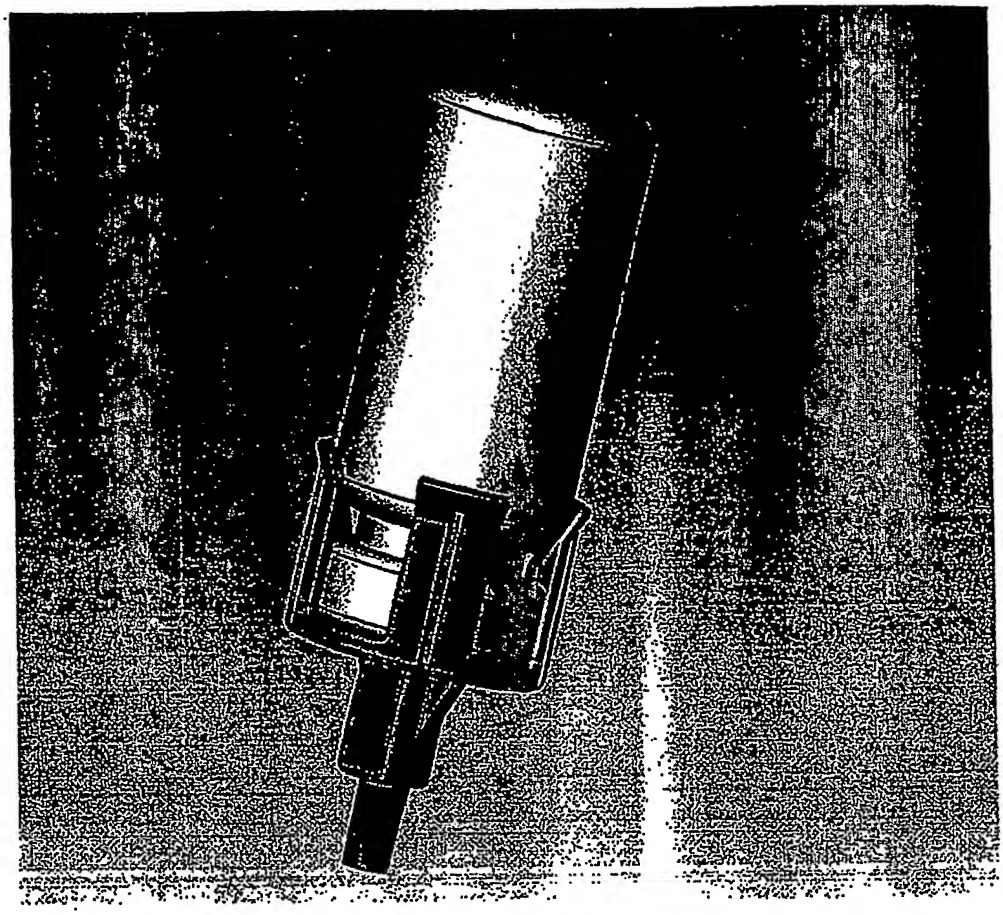


Figure 3.

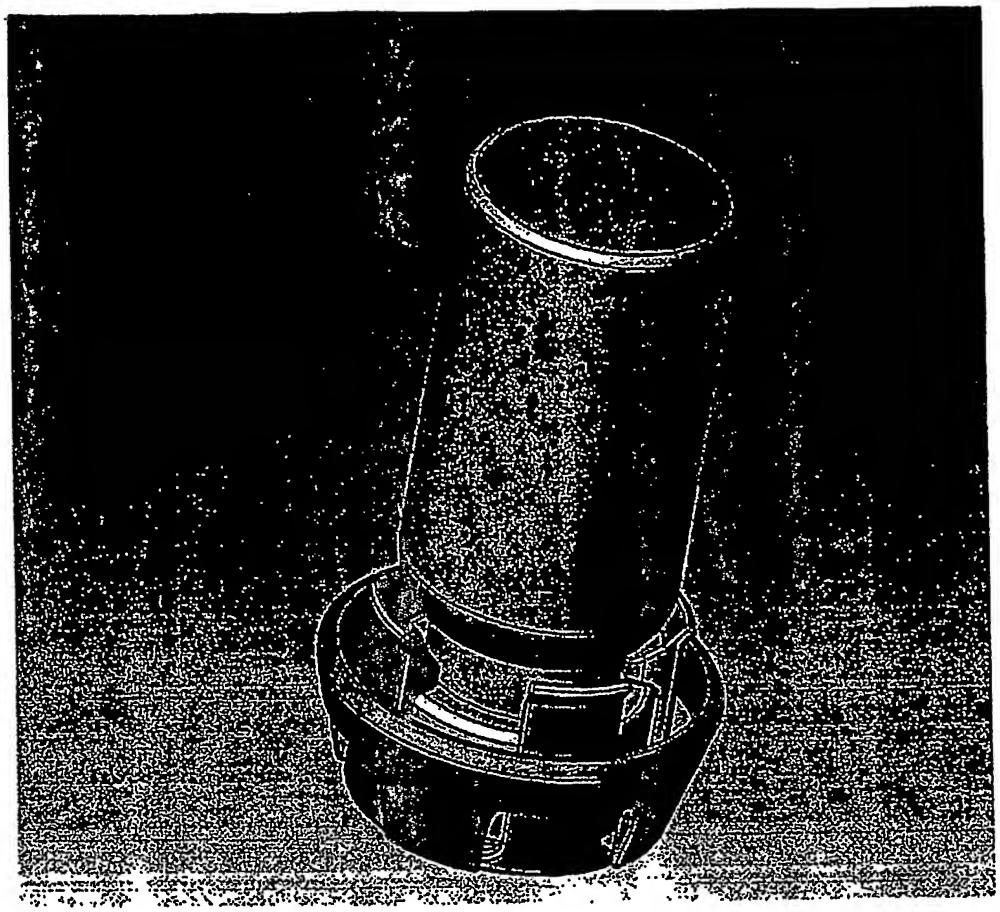


Figure 9

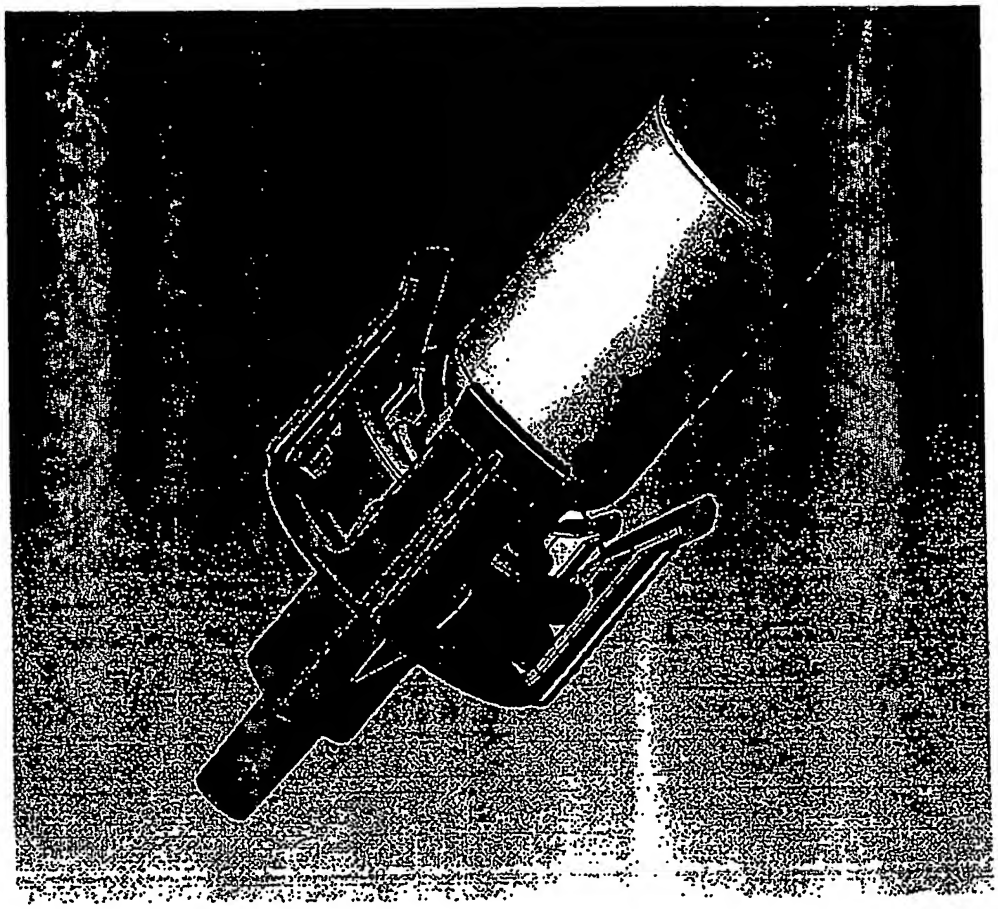


Figure 10

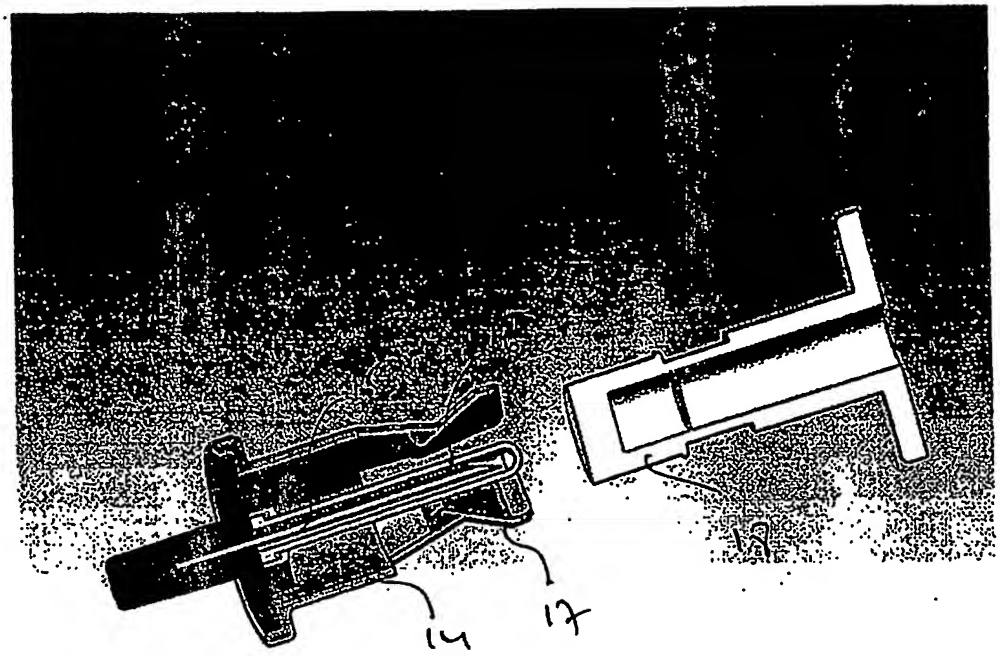
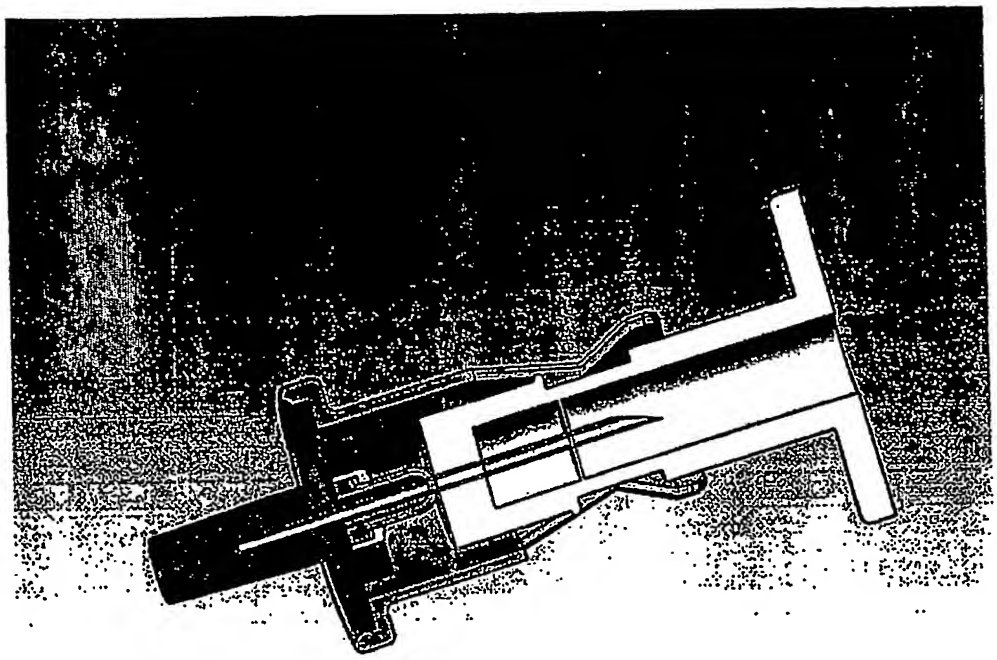


Figure 11.



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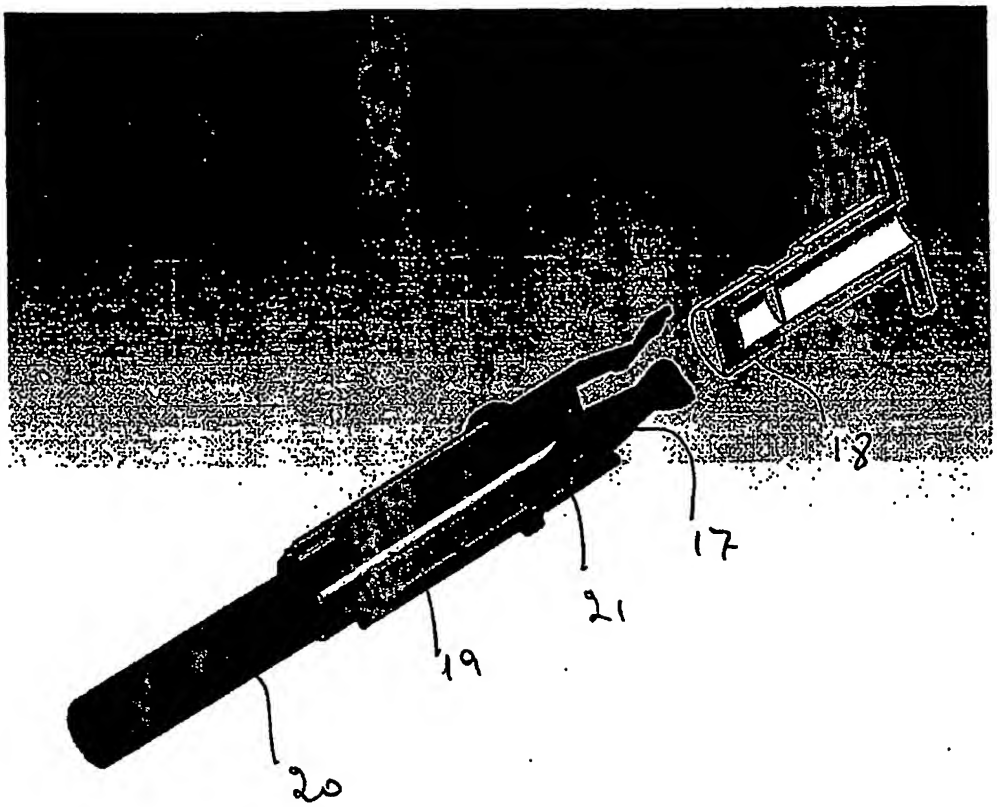

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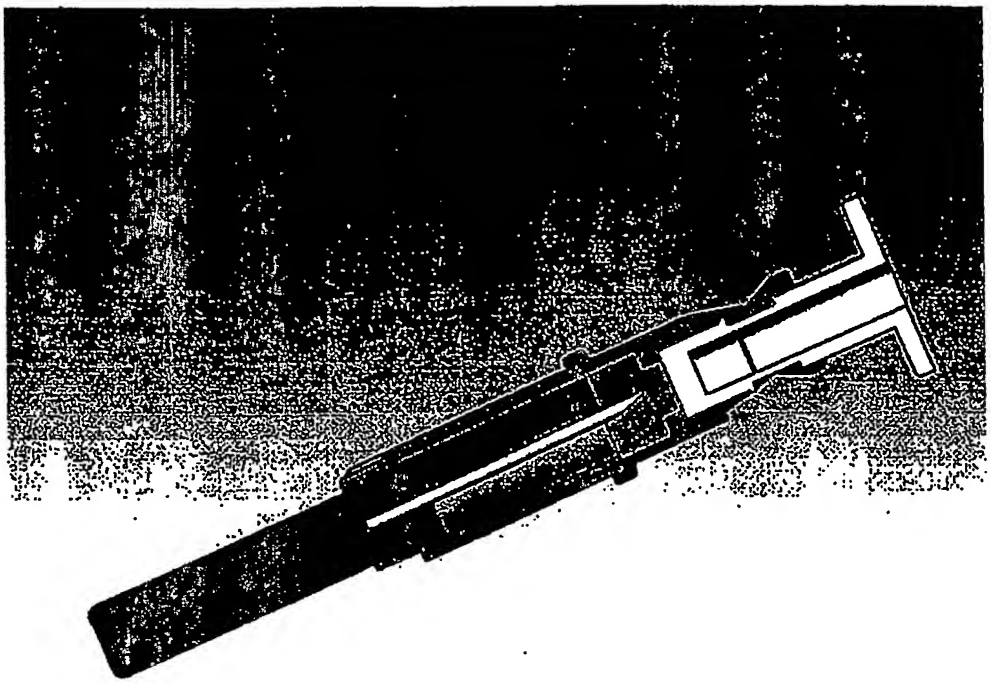


Figure 14

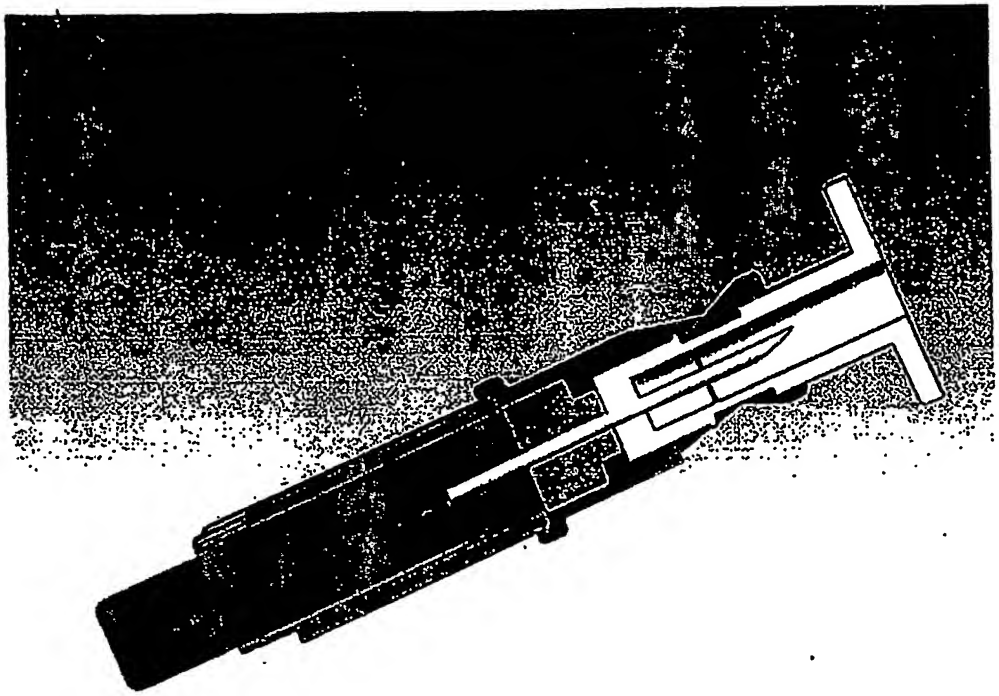


Figure 15

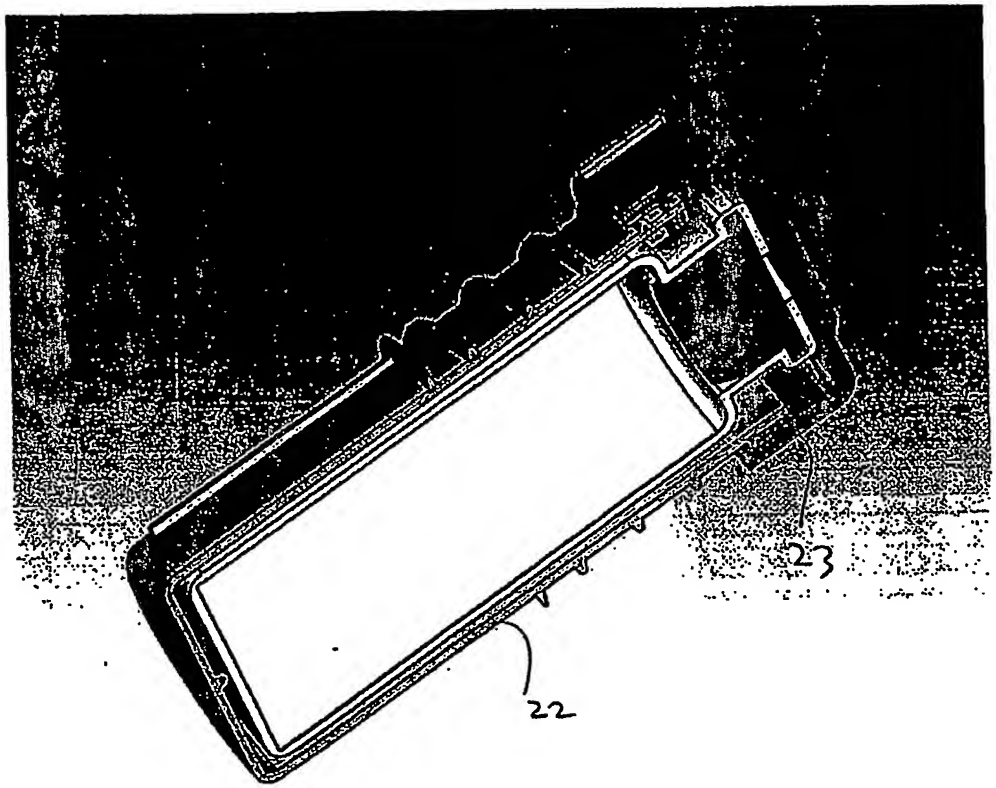
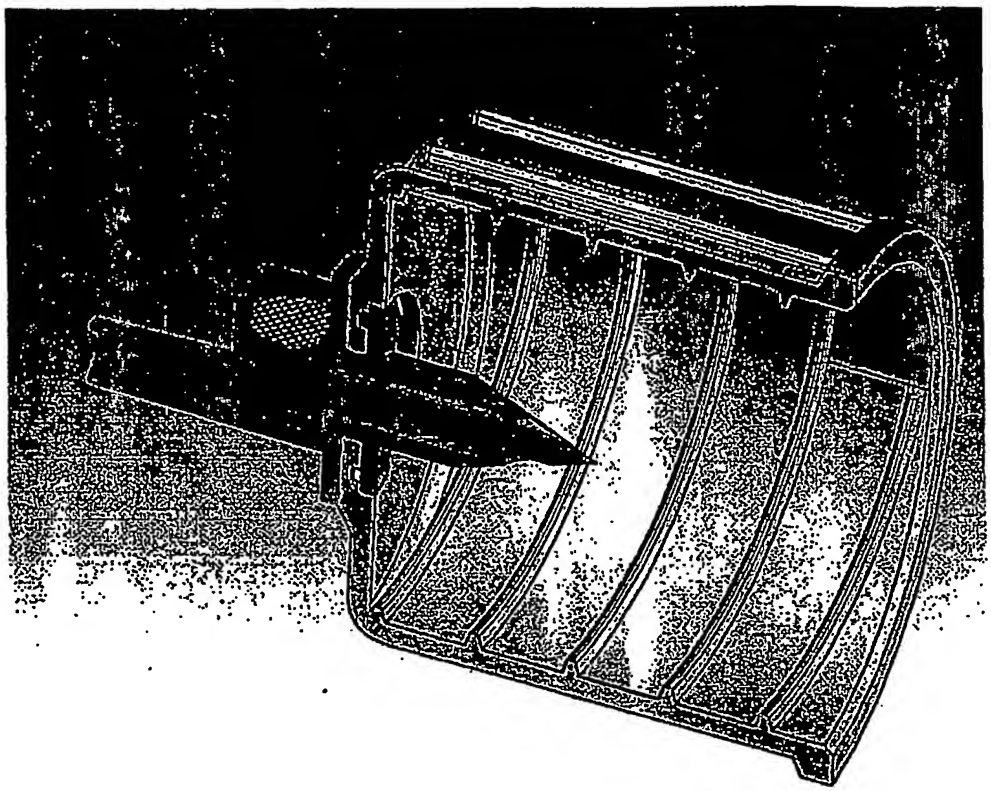


Figure 16



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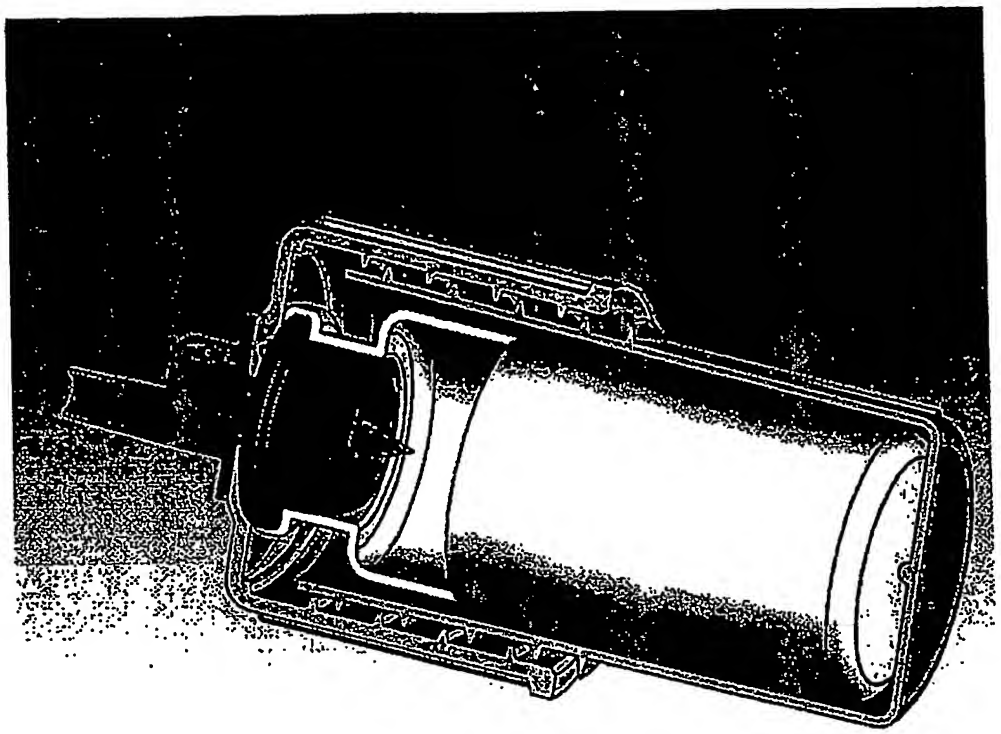

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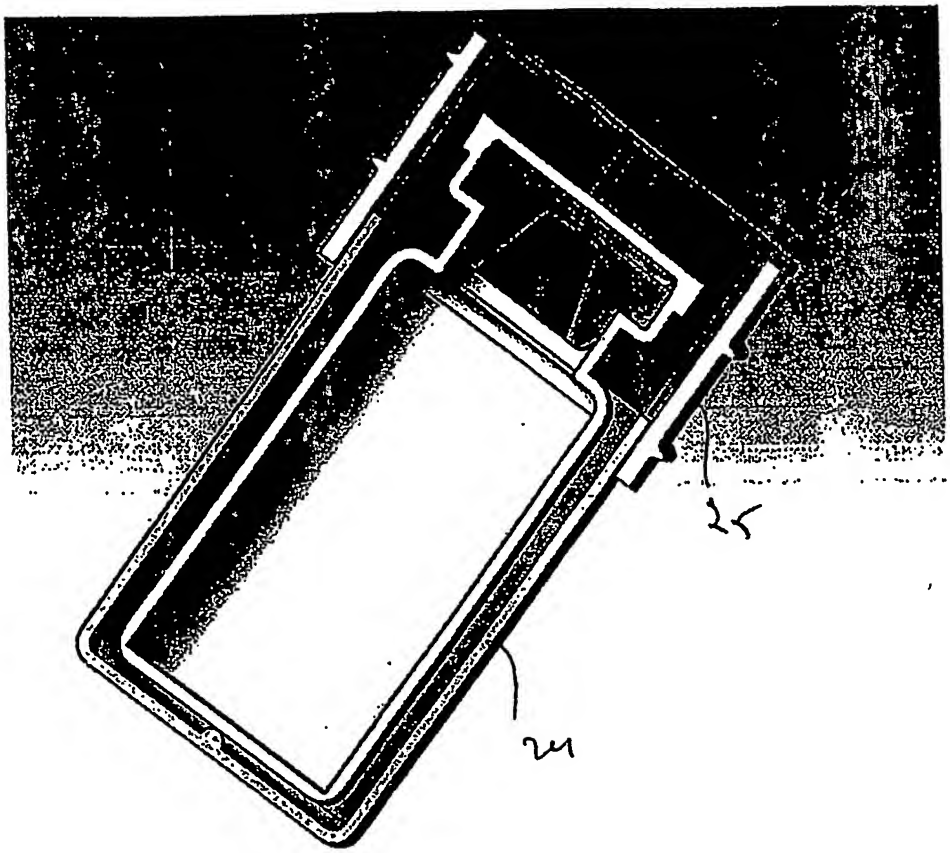

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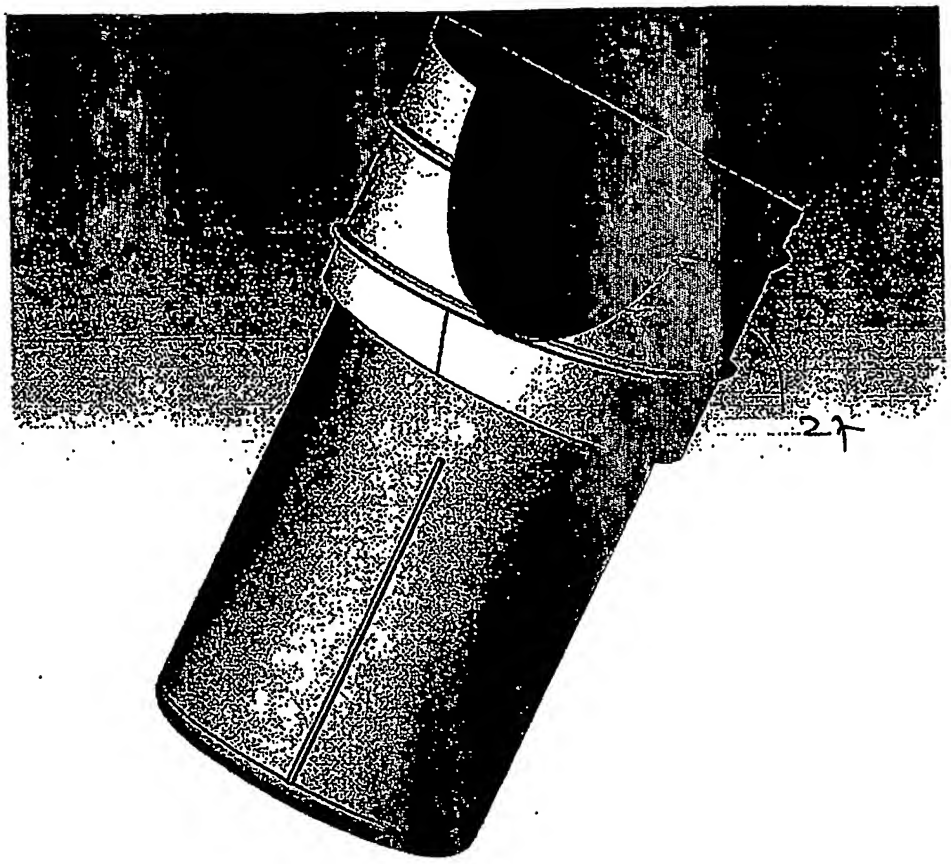

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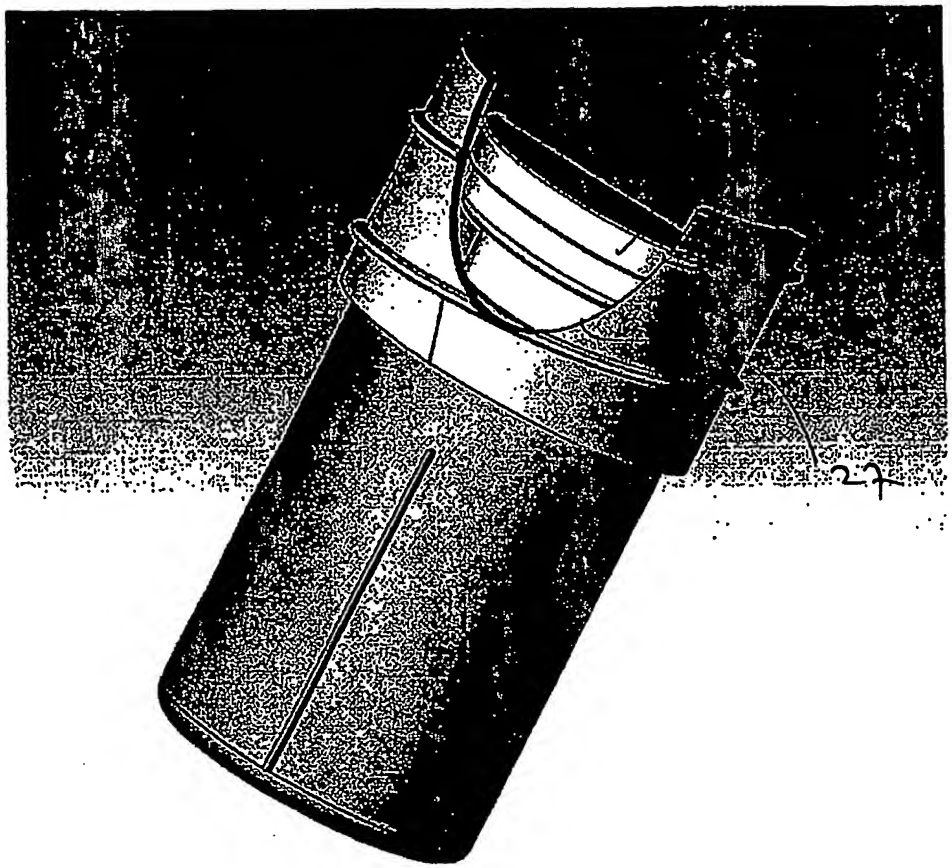

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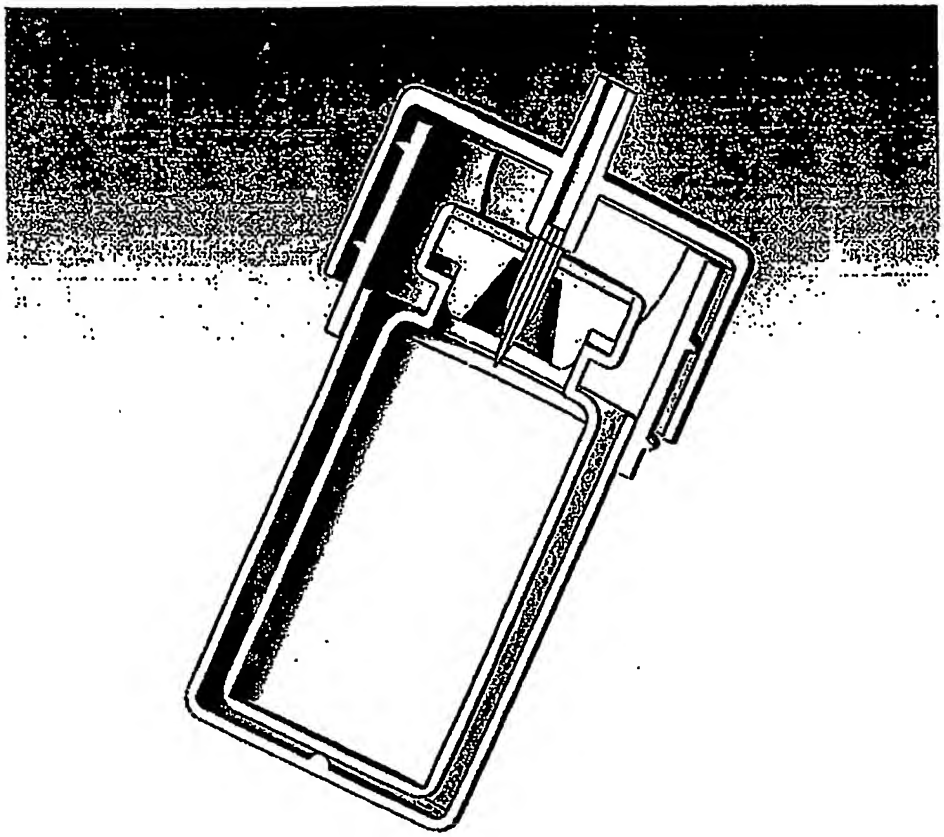

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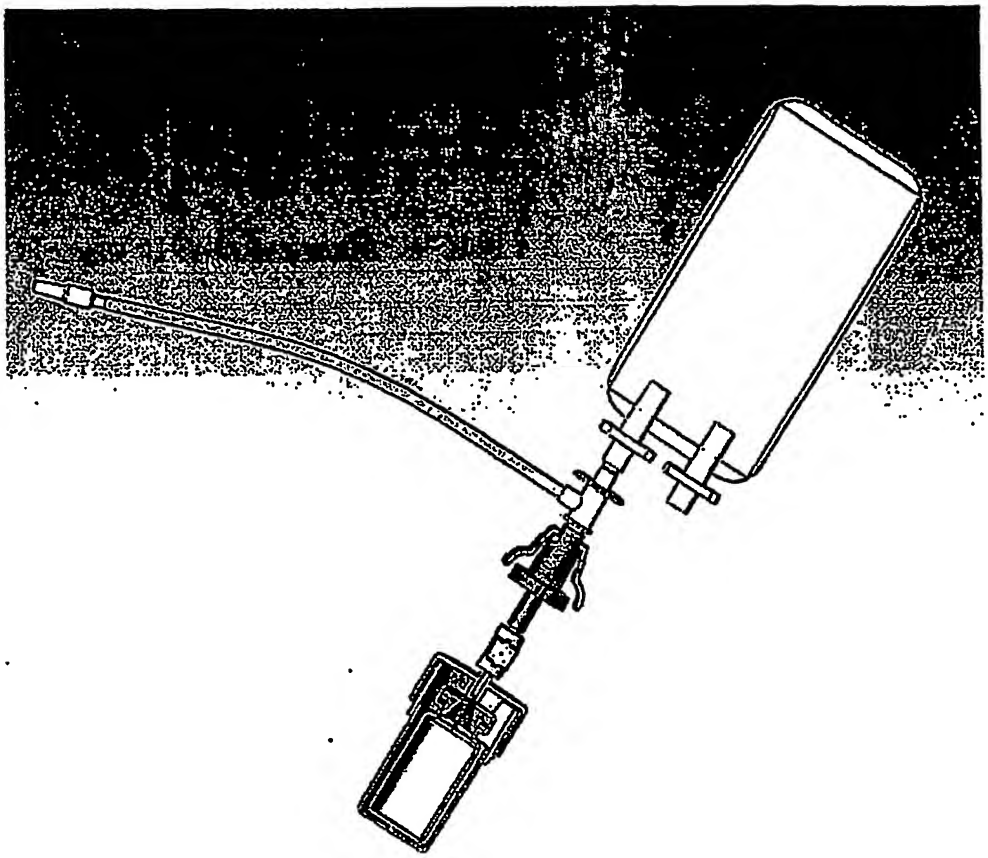

Figure 23

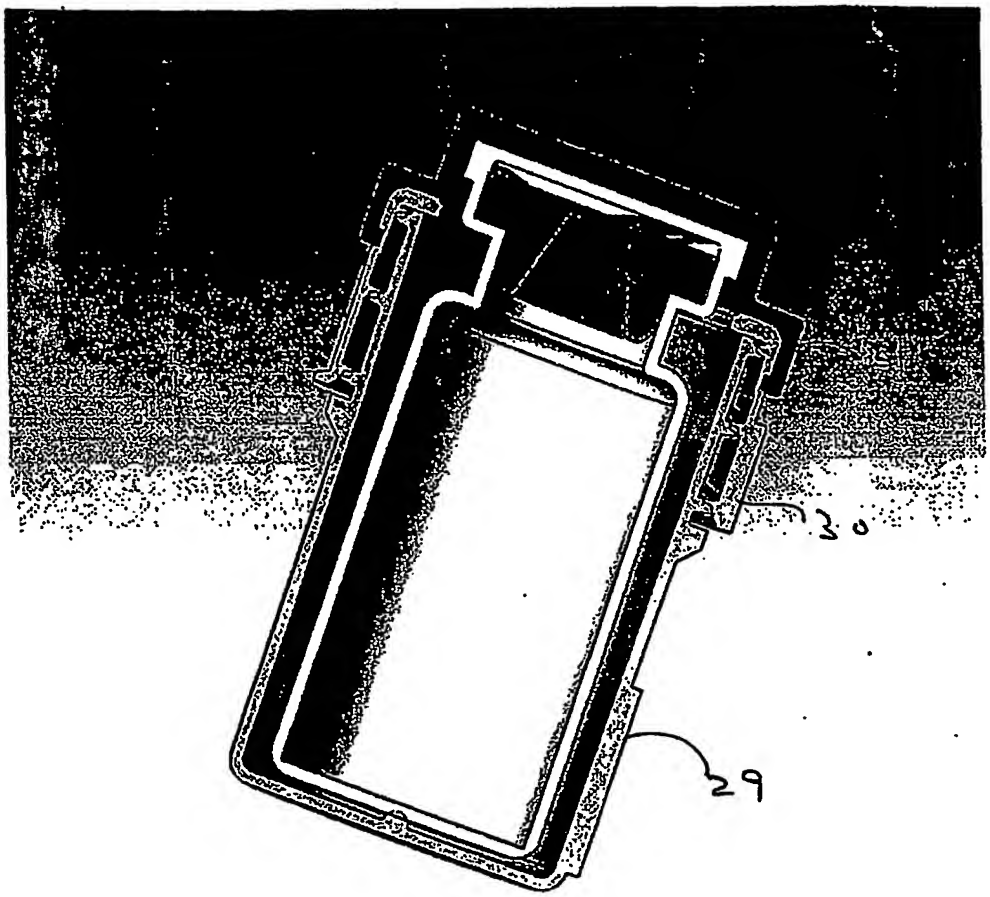

Figure 2a

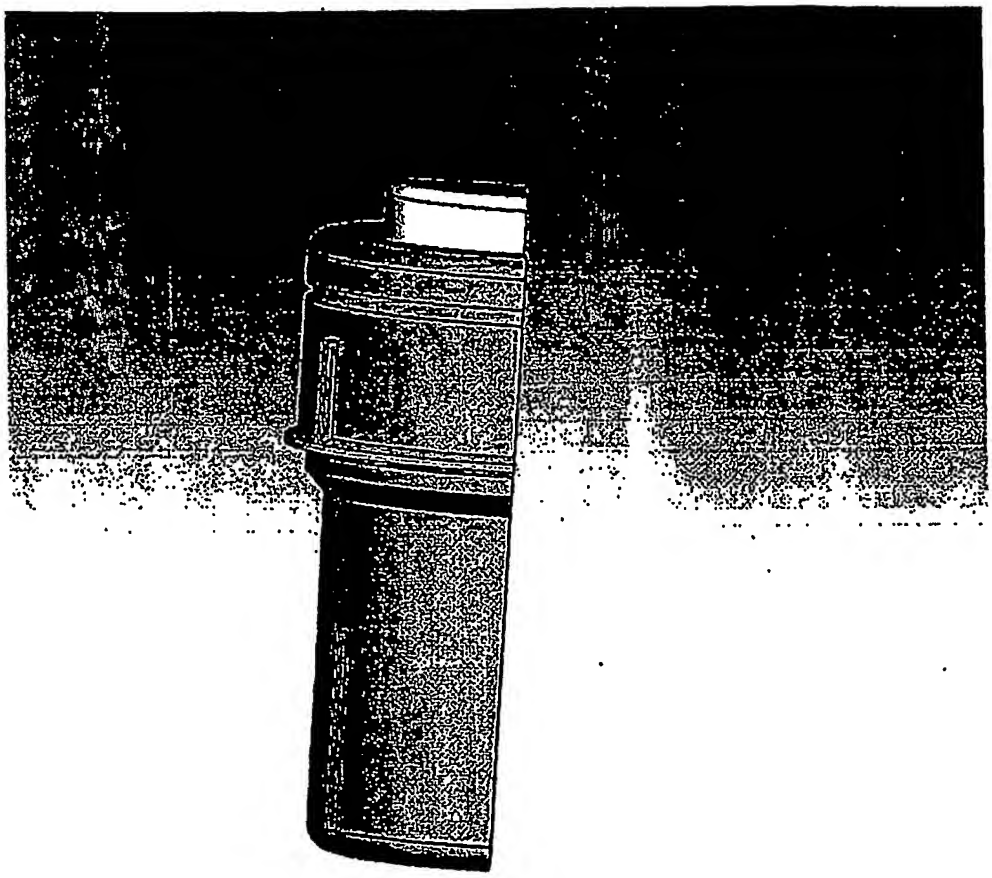

Figure 2

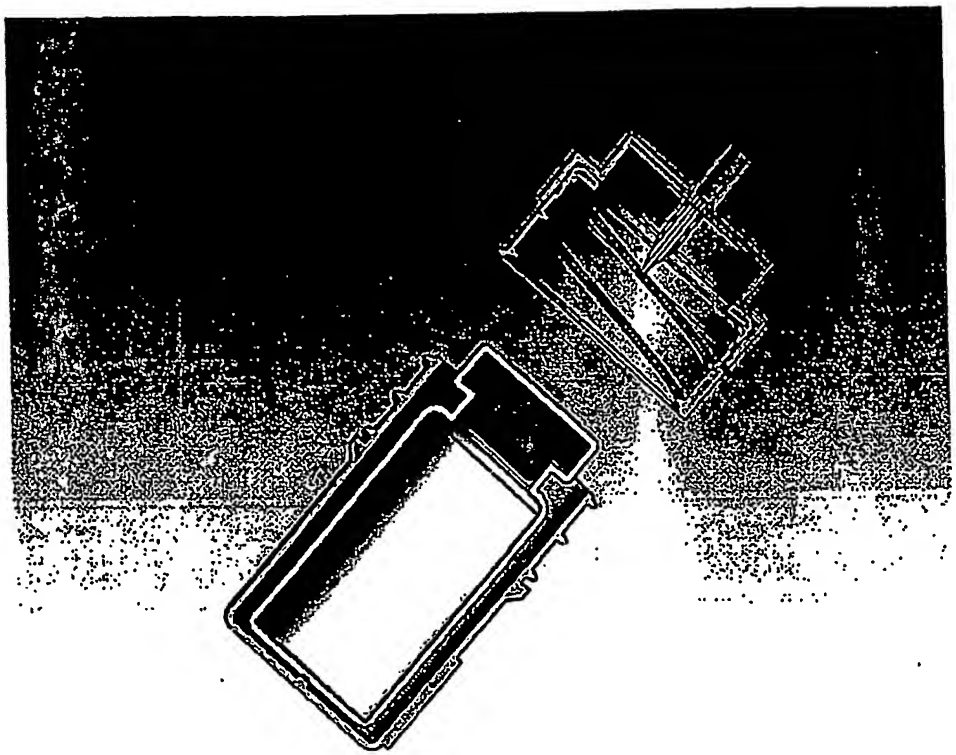

Figure 26

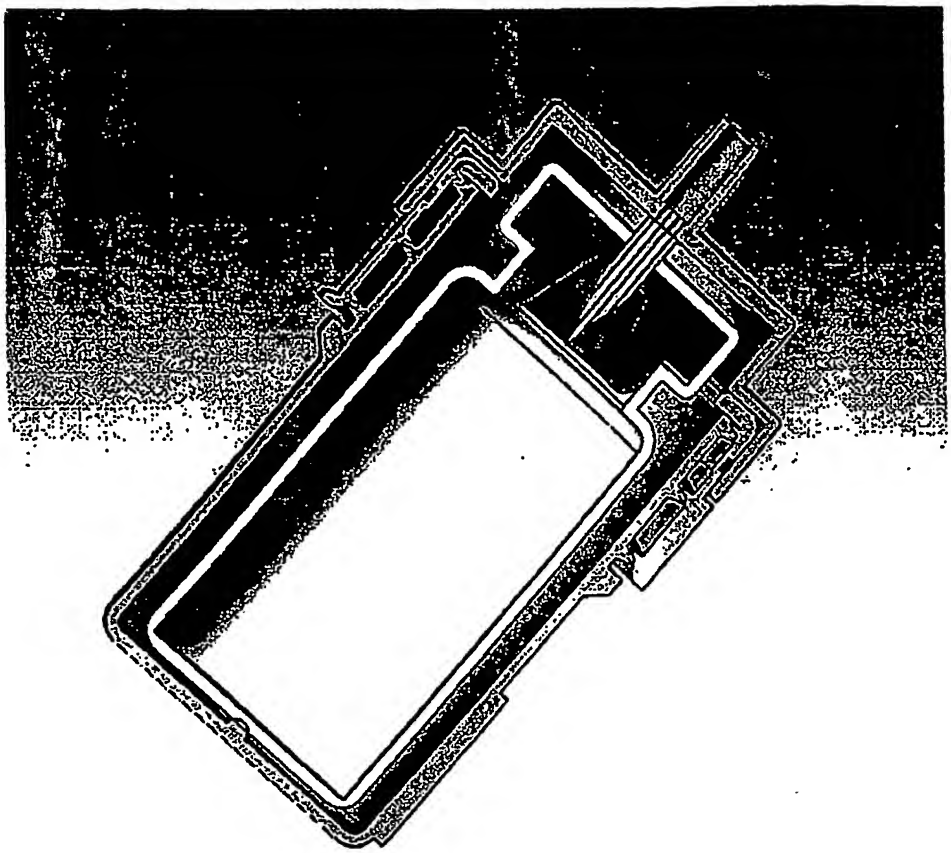

Figure 27

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